

additional sites for incorporating substances. Matrix materials such as collagen in a gelatin form may be used to improve the ability of the material to dissolve. Acid extraction method can be used in preparing such gels to maintain the structure of the monomeric subunits. Units can then be treated with enzymes to alter the structure of the monomers.

In embodiments in which two materials combine to form a third material, the solutions containing these components can be mixed together immediately before they are streamed from an orifice in the electroprocessing procedure. In this way, the third material forms literally as the microfibers or microdroplets are formed in the electrospinning process. Alternatively, such matrices can be formed by electrospraying a molecule that can form matrix materials into a moist or otherwise controlled atmosphere of other molecules necessary to allow formation of the matrix to form filaments within the electric field. For example, fibrinogen can be sprayed into a moist atmosphere of thrombin. Materials such as fibrinogen that are capable of forming other materials such as fibrin can also be electrosprayed onto a target that has thrombin. Alternatively thrombin can also be electrosprayed onto a target that has fibrinogen.

In embodiments in which two or more matrix materials are combined to form a third (for example, combining fibrinogen and thrombin to form fibrin) the matrix materials can be electroprocessed in conjunction with or separately from each other, typically under conditions that do not allow the two molecules to form the third until the desired time. This can be accomplished several ways. Using fibrinogen and thrombin as an example, the two matrix materials can be electroprocessed from a solvent that does not allow thrombin to function. Alternatively, the fibrinogen or thrombin can be packaged in a carrier material. In this application the fibrinogen is electroprocessed onto the target from one solution source (by itself or with a carrier), and the thrombin is deposited in an electroaerosol manner from a separate source. The thrombin can be encapsulated and sprayed as a fine mist of particles. Alternatively, thrombin and fibrinogen can be mixed with a carrier, such as PEG, or other synthetic or natural polymers such as collagen. The carrier acts to hold the reactants in place until they are initiated. These methods are not limited to thrombin and fibrinogen and also are used with embodiments involving other combinations of matrix materials that combine to form a third material. The entire product is preferably stored under dry conditions to prevent the reaction of the two materials. When the material is

placed in a moist environment, the materials are able to combine and the product matrix material is formed.

As stated above, it is to be understood that carriers can be used in conjunction with matrix materials. Different materials, such as extracellular matrix proteins, and or substances, can be mixed with PEG or other known carriers that form filaments. For example, fibrinogen and collagen can be mixed with PEG or other known carriers that form filaments. This produces "hairy filaments" with the hair being fibrin. The "hairs" cross-link the surrounding matrix carrier into a gel, or provide reactive sites for cells to interact with the substance within the matrix carrier, such as immunoglobulins. This approach can be used for forming a matrix or gelling molecules that do not normally gel. For example, in embodiments in which a specific type of matrix material will not form filaments, then the matrix material can be combined with fibrin and PEG and electrosprayed to form an electroprocessed fibrin-containing matrix. Once fibrin formation begins, a gel of the matrix material and fibrin together is produced.

Alternatively, the material can be sputtered with another molecule that forms a sheet. Examples of molecules that form sheets include PGA, PLA, a copolymer of PGA and PLA, collagen, and fibronectin. In some embodiments, a sheet is formed with two or more materials that can combine to form a third material. This sheet can be placed in a wet environment to allow conversion to the third material.

In addition to the multiple equipment variations and modifications that can be made to obtain desired results, similarly the electroprocessed solution can be varied to obtain different results. For instance, any solvent or liquid in which the material is dissolved, suspended, or otherwise combined without deleterious effect on the process or the safe use of the matrix can be used. Materials or the compounds that form materials can be mixed with other molecules, monomers or polymers to obtain desired results. In some embodiments, polymers are added to modify the viscosity of the solution. In still a further variation, when multiple reservoirs are used, the ingredients in those reservoirs are electrosprayed separately or joined at the nozzle so that the ingredients in the various reservoirs can react with each other simultaneously with the streaming of the solution into the electric field. Also, when multiple reservoirs are used, the different

ingredients in different reservoirs can be phased in temporally during the processing period. These ingredients may include substances.

Embodiments involving alterations to the electroprocessed materials themselves are within the scope of the present invention. Some materials can be directly altered, for example, by altering their carbohydrate profile. Also, other materials can be attached to the matrix materials before, during or after electroprocessing using known techniques such as chemical cross-linking or through specific binding interactions (e.g. PDGF binds to collagen at a specific binding site). Further, the temperature and other physical properties of the process can be modified to obtain different results. The matrix may be compressed or stretched to produce novel material properties.

Still further chemical variations are possible. Fibrin, for example, is formed in different ways. Building an electroprocessed matrix comprised of fibrin, therefore, involves different ways of bringing the molecules capable of forming fibrin, such as fibrinogen and thrombin, together through electroprocessing methods. Electroprocessed materials and matrices can also be manipulated after they are formed with the electroprocessing methods.

A matrix of electroprocessed fibers, in accordance with the present invention, can be produced as described below. In the case of electrospun fibrin, while any molecules capable of forming fibrin can be used, it is preferable to electroprocess fibrinogen or thrombin to make fibrin fibers.

Electroprocessing using multiple jets of different polymer solutions and/or the same solutions with different types and amounts of substances (e.g., growth factors) can be used to prepare libraries of biomaterials for rapid screening. Such libraries are desired by those in the pharmaceutical, advanced materials and catalyst industries using combinatorial synthesis techniques for the rapid preparation of large numbers (e.g., libraries) of compounds that can be screened. For example, the minimum amount of growth factor to be released and the optimal release rate from a fibrous polymer scaffold to promote the differentiation of a certain type of cell can be investigated using the compositions and methods of the present invention. Other variables include fiber diameter and fiber composition. Electroprocessing permits access to an array of samples on which cells can be cultured in parallel and studied to determine selected compositions which serve as promising cell growth substrates.